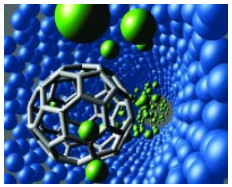


NANOTECHNOLOGY

Navy Occupational Health and Preventive Medicine Conference

Presenters:

Linda A. McCauley, PhD, RN, FAAN

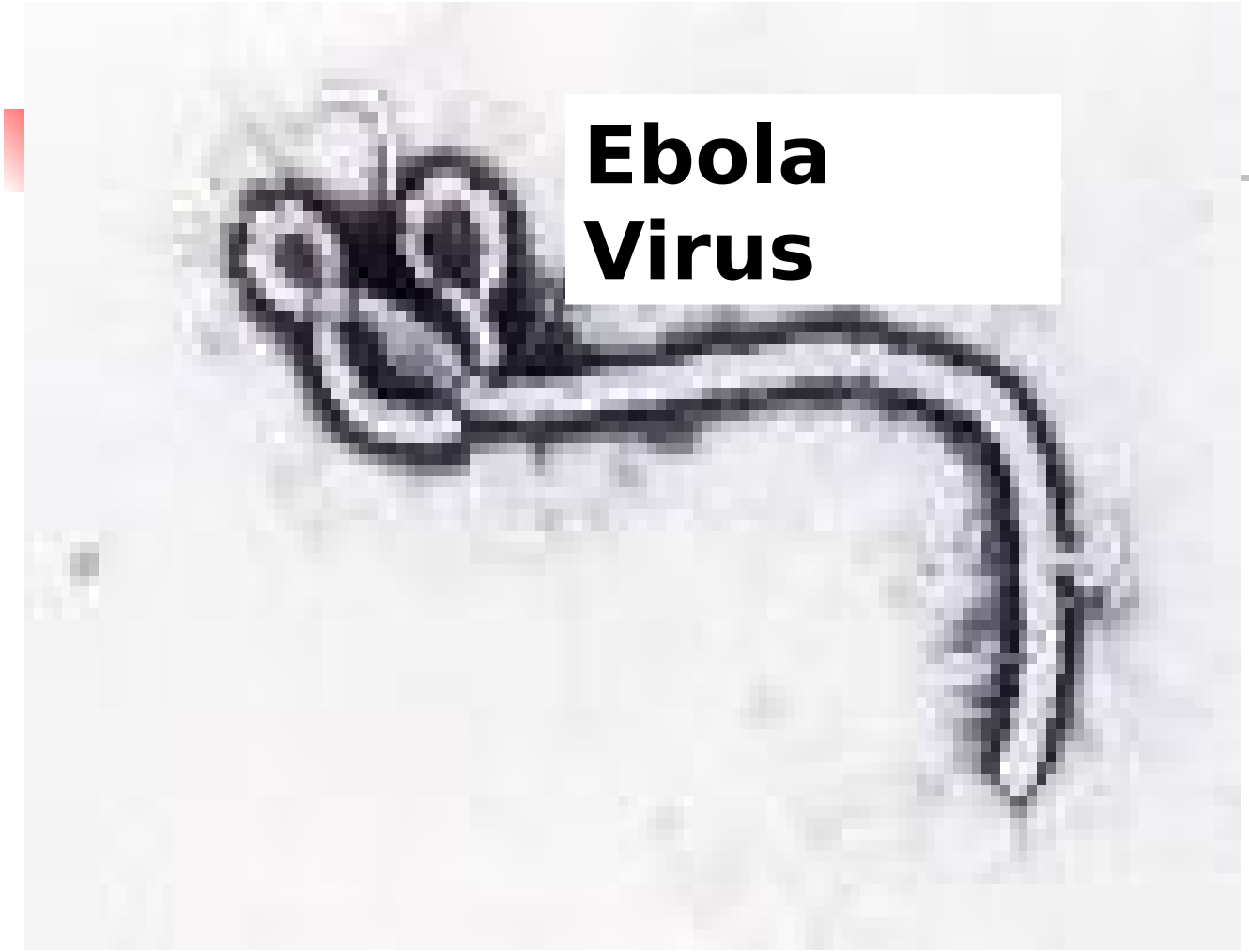
Ronald D. McCauley, MBA

Presentation Outline

- Nanotechnology Defined & Introduction
- Context: Products and Applications
- The Business and Economics of Nanotech
- Occupational Health Concerns
- Environmental Health Concerns
- Projected Military Applications
- Recent Nanotech News
- Public Resources for Further Study

Nanomaterials Defined

- Structures or devices assembled at the atomic level
  - Size measured in Billionths of a Meter (nano)
  - Have at least one dimension of 100 nanometers or less (roughly 1/10 the size of an Ebola virus)
  - 100 Nanometers is about 1/500th the width of a human hair



Rhinoviru
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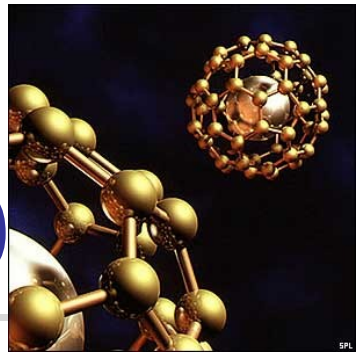
The First Vision: 1959



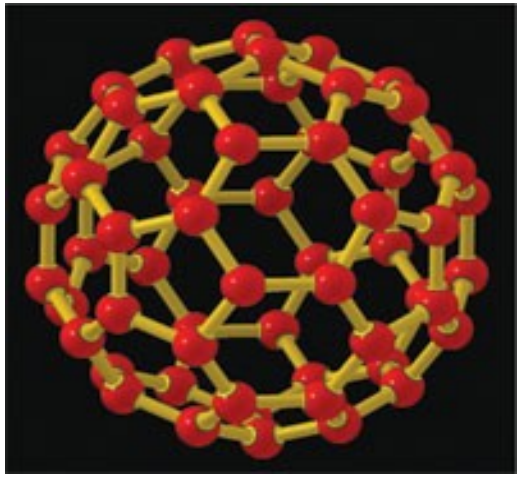
Nobel Laureate Richard Feynman:

"The principles of physics, as far as I can see, do not speak against the possibility of maneuvering things atom by atom."

Lecture given at annual meeting of the American Physical Society at the California Institute of Technology
December 29, 1959

Buckminster Fullerene C_{60} Discovered in 1985

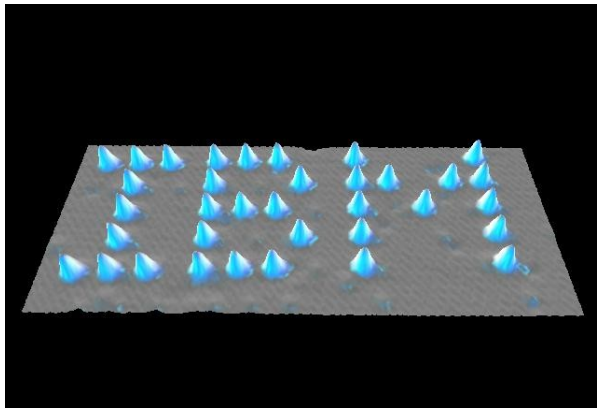
- Naturally occurring but manufactured in mass quantity now
- Named after Buckminster Fuller due to the structural similarity to his Geodesic Dome design



“BUCKYBALL”

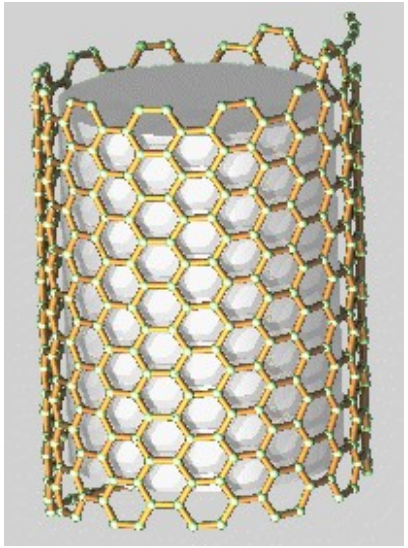
Assembly at Atomic Level

1990: Scanning Tunneling technology used by Don M. Eigler and Erhard K. Schweizer to create the IBM logo using 35 Xenon atoms. Each letter is about 5nm in height.

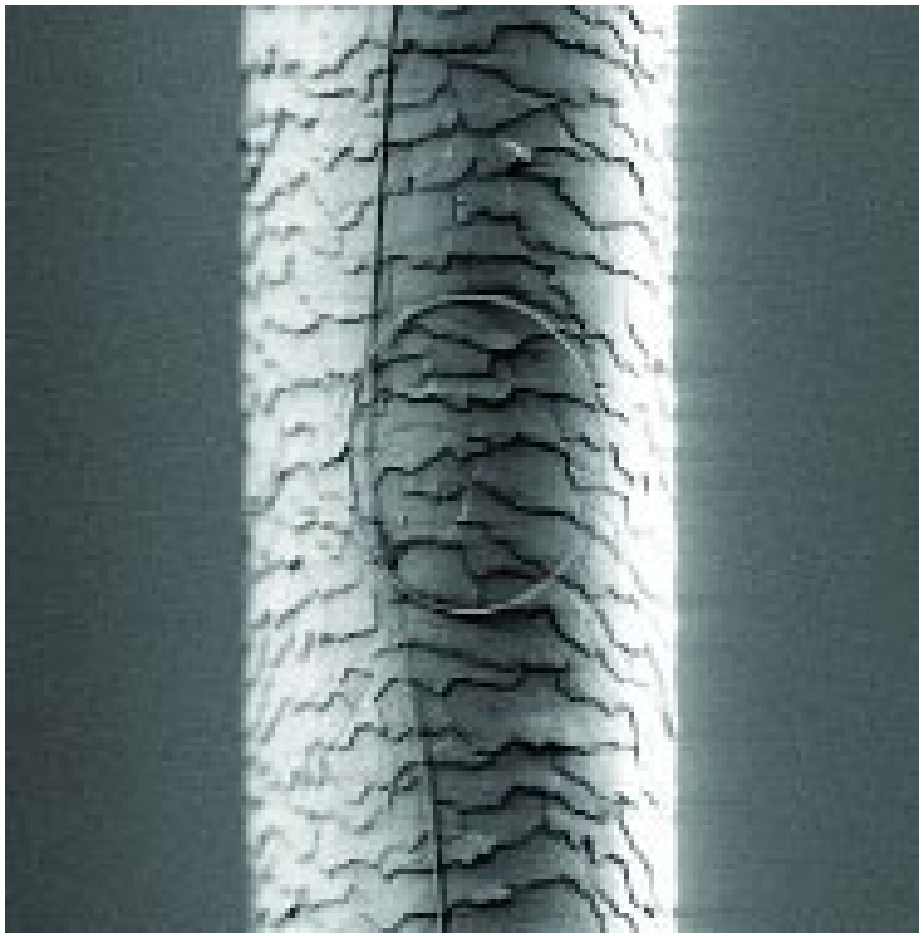


Other “Fullerenes”

- “Nanotube” discovered in 1991
  - A nanoscale carbon sheet that folds in upon itself

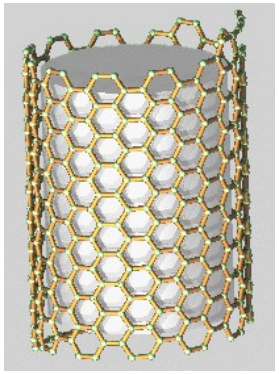


Nanowire In Front of a Human Hair



Why Nanomaterials?

- Unique Chemical, Physical and Electrical Properties:
  - For Example: Nanotubes are stronger than steel, but lighter than aluminum
    - Can act as conductive wires or semiconductors
    - Can transport heat or electricity with little resistance
    - Can be made to emit light
    - Can be woven into fabrics



Fullerene Nanoparticle Production

- Bulk processes through high temperature combustion
- Companies in Japan and U.S. producing nano-materials by the ton
- Nano-particles are then purchased by other companies for use in products
- Products do not regularly disclose nano-material contents

Nanomaterial Applications

- Many already on the market:
  - Cosmetics, sunscreen, sporting goods, stain-resistant clothing, electronics, sensors, anti-microbial agents, paints, food supplements, …
- Coming Soon:
  - Pharmaceuticals – drug delivery
  - Tumor targeting cancer treatments
  - Artificial Bone composites
  - Catalytic materials (I.E. chemical spill clean-up), Industrial films, Building materials/Insulation, many more
- Foreseeable Future:
  - Fuel Cells, Solar Cells, Batteries, nano-scale devices and machinery

Source: Nanotechnology Information Center, americanelements.com/nanotech.htm

- Is anyone here aware of personally using products containing nano-particles?

Current consumer products allegedly using nanotechnology

MAYNARD, A. D. Ann Occup Hyg 2007 51:1-12; doi:10.1093/annhyg/mel071

The Annals of Occupational Hygiene

Nanomaterials and some Current Products

- **Fullerenes and Carbon Nanotubes**: Fabrics, Cosmetics, Electronics, Sports Equipment, Lubricants, Building Materials, Food Supplements, Food Flavorings
- **Silver**: Antibacterials, Antifungals, Self-Cleaning Glass, Spermicidal Condoms, Food Storage Containers, Air Sanitizer Sprays and Air Filtration, Hygiene Products, Bandages
- **Silica**: Electronics, Paints/Pigments, Cosmetics, Food Supplements
- **Zinc Oxide and Titanium Oxide**: Clear – thin film sunscreens, Cosmetics, Self-Cleaning Coatings, Lens Defoggers
- **Gold**: Chemical Detection, Home Pregnancy Tests, Wrinkle Reducing Skin Cream

Nano-Bandage

Curad® Silver Bandages:
"…use silver in the wound pad as a natural antibacterial. Laboratory testing showed that silver reduced bacterial growth like *Staph. aureaus, E. coli, E. hirae and Pseudomonas aeruginosa* (a powerful germ that does not respond to many antibacterials) in the dressing for 24 hours."

Nano-Laundry:

Samsung Silvercare™ Washing Machine

- Electrical currents “nano-shave” two silver plates.
- Positively charged silver ions are injected into the wash water.
- According to tests, this process removed or killed 99.9% of odor-causing bacteria.

Nano-Clothing

NANO-TEX™:
“Resists Spills … makes you look and feel great all day. Liquid and oil based spills like red wine, juice, and salad dressing bead up and roll off without soaking in.”

Eddie Bauer
EST. 1920

Global Investment Share in Nanotech Research to Date

- U.S. 28%
- Western European Countries: 25%
- Japan: 24%
- China, South Korea, Canada, Australia and others: 23%

Source: Business Wire, Feb. 22, 2007, Galenet.galegroup.com

Some Potential Dangers of Technology being discussed in the "Nano-community"

- Increased Inflammatory Response in the Body and the Environment due to Small Size
- What Regulations would be effective? What Agency should be in charge of Regulations?
- Economic disruption due to new range of products and manufacturing technology
- Potential terrorist use
- Social disruption from new products/lifestyles
- New Arms Race
- Environmental Damage from Unregulated products
- "Grey Goo" Scenario (Free range self-replicators)
  - Center for Responsible Nano-Technology

Nanomaterial Economy

- Estimated to be worth $1 Trillion to the U.S. economy by 2015
- More that 2 Million jobs expected to support nanotech industries
- Over 1,700 organizations worldwide are actively engaged in “nano-research” (nanovip.com)
- Expected proliferation into virtually every aspect of commerce
- Products containing nanomaterials predicted to be worth $292 Billion by end of this decade

Nanomaterial Economy Cont.

- A Sample of Industries Projected to Experience Economic Disruption (in Billions):
  - Healthcare: $1,700
  - Electronics: $550
  - Telecom: $550
  - Plastics: $460
  - US Chemical: $450
  - Apparel: $182
  - Pharmaceutical: $180

Source: Nanotechnow.com

Enabling the “Hydrogen Economy?”

- Electrochemical Storage of Hydrogen in Carbon Nanotubes
  - Nano Science and Technology Institute www.nsti.org
- Sunlight to Fuel Hydrogen Future
  - “…metal oxide particles that are less than 30 nanometers thick and can convert sunlight energy into hydrogen…”
    - Wired News www.wired.com

Nanotech Companies

- Many of the usual suspects from among the Fortune 500:

Nanotech Companies

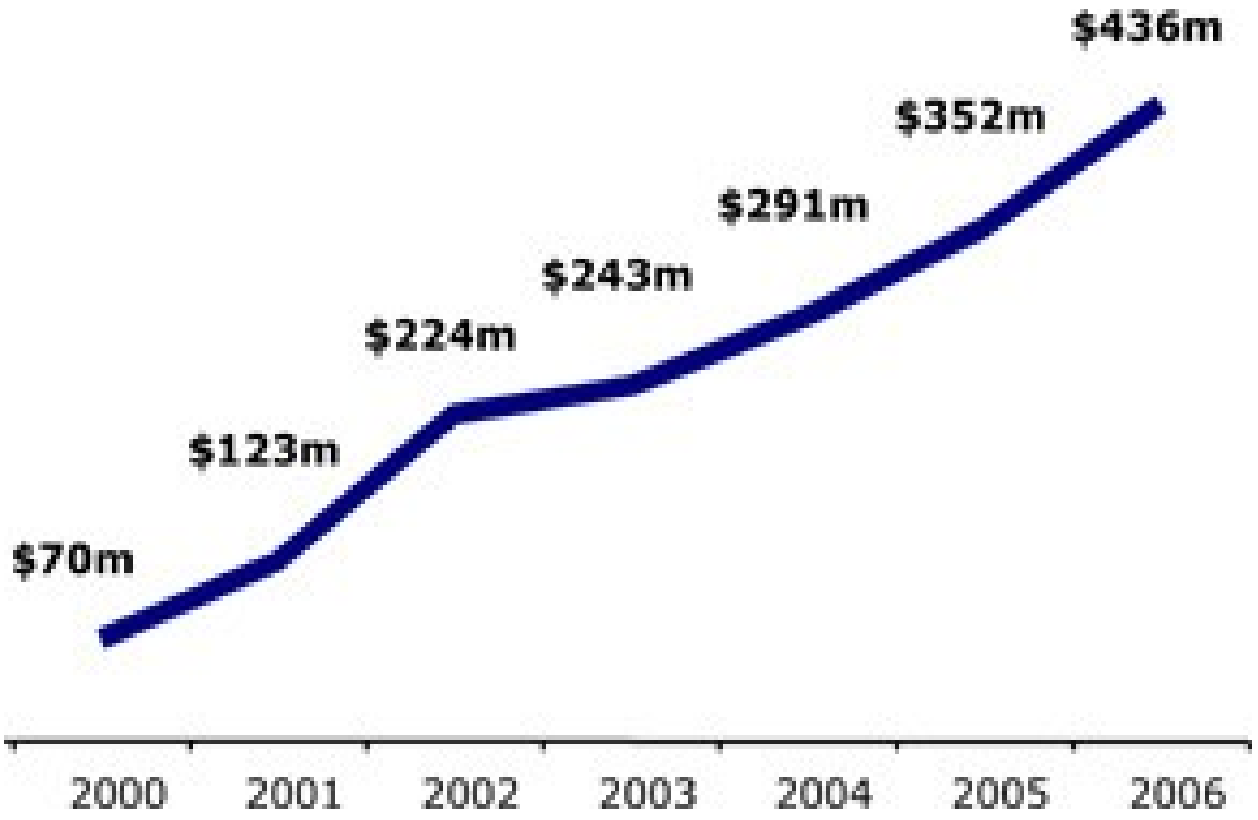
- Many nano-industry specialists you probably don't know:

That Washing Machine

- EPA on Nov. 21, 2006:
  - The Samsung silver ion generating washing machine, which releases nano silver ions into wash water, is subject to registration requirements under the Federal Insecticide, Fungicide and Rodenticide Act, or FIFRA.

Annual DoD Investment in Nanotechnology; 2006 estimated.

(DoD "Defense Nanotechnology Research and Development Programs", May 8, 2006)



Future Warrior of 2025

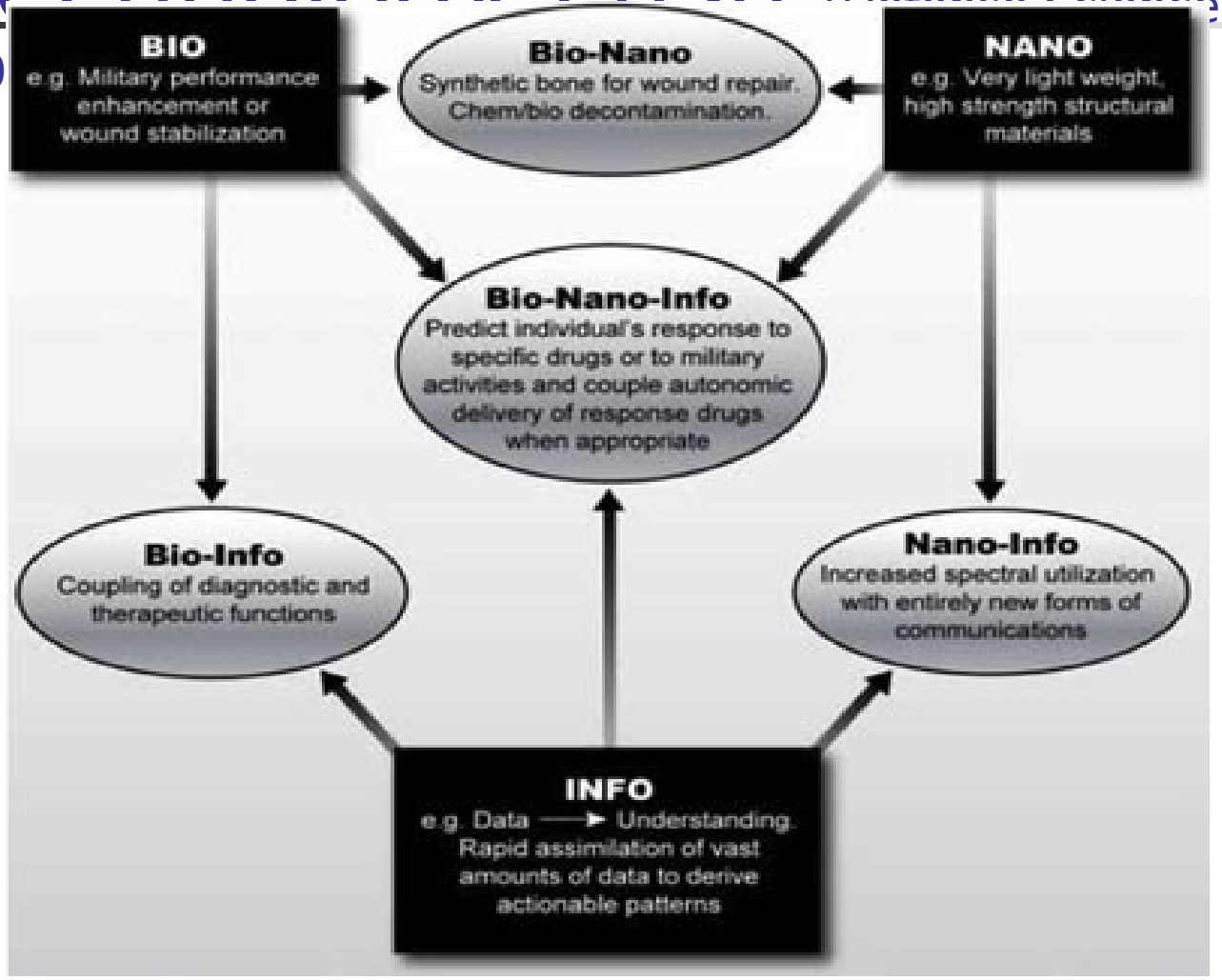
Nano-Applications Under Development by Army and MIT

An integrated technology system with:

- Ballistic protection
- Communications/Information system
- Chem/Bio protection
- Power
- Climate Control
- Strength Augmentation
- Physiological Monitoring
- Three-Layer Bodysuit and Headgear System

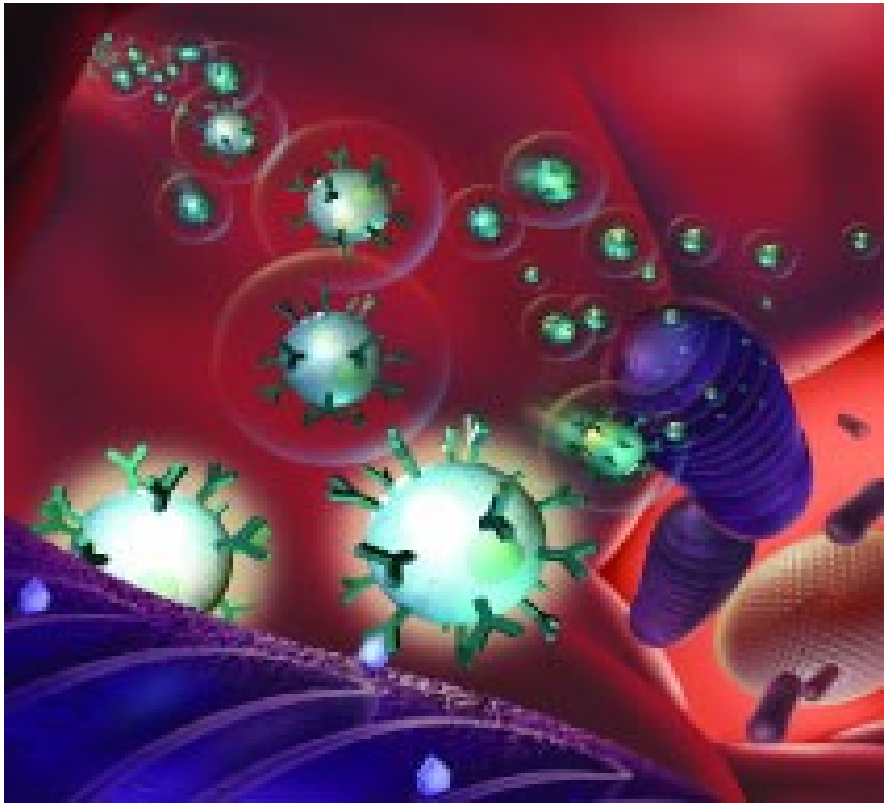
(Source: MIT's Institute for Soldier Nanotechnologies)

DoD Game Changing Technology Push (Defense Science Board, 20


BIO
e.g. Military performance enhancement or wound stabilization
Bio-Nano
Synthetic bone for wound repair. Chem/bio decontamination.
NANO
e.g. Very light weight, high strength structural materials
Bio-Nano-Info
Predict individual's response to specific drugs or to military activities and couple autonomic delivery of response drugs when appropriate
Bio-Info
Coupling of diagnostic and therapeutic functions
Nano-Info
Increased spectral utilization with entirely new forms of communications
INFO
e.g. Data ⟶ Understanding. Rapid assimilation of vast amounts of data to derive actionable patterns

NCI Nanotechnology Alliance: http://nano.cancer.gov/

Nanoparticle Probes



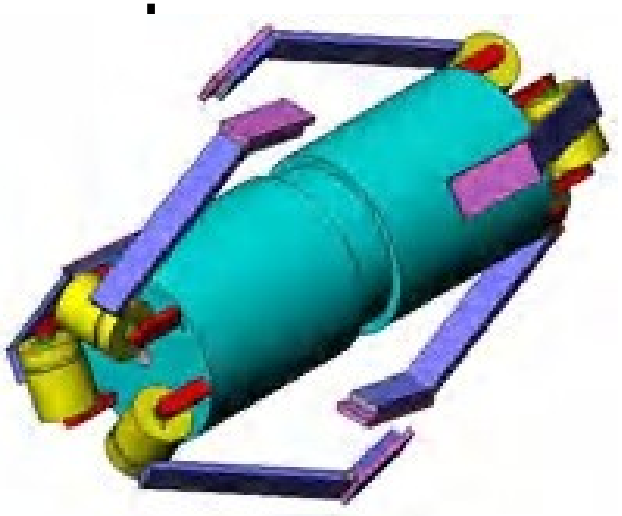
- Antibody-labeled quantum dots traveled through the bloodstream to tumors in mice. The antibody then binds with proteins found on the surface of the tumor.

Use in Stem Cell Research: 2/27/07

- Distinct perfluorocarbon nanoparticles were used to track different stem cells injected into tumor-bearing mice. These particular nanoparticles are taken up readily by stem cells over the course of a 12-hour incubation, and the stem cells showed no ill effects from the nanoparticles

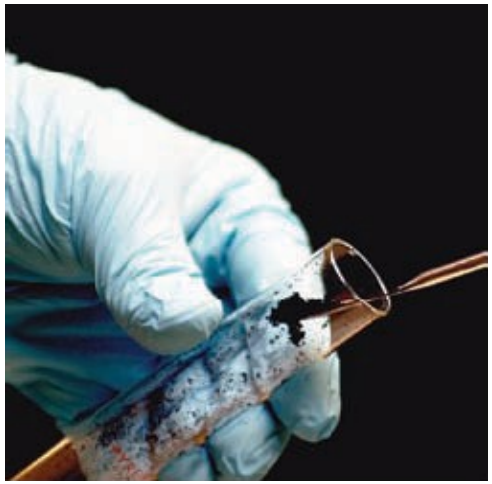
Mechanical Engineering and Medicine Produces Nano-Robotics

- Concept of Endoscopic Microcapsule
- Swallowable imaging ‘pill’ and new endoscopic instrun



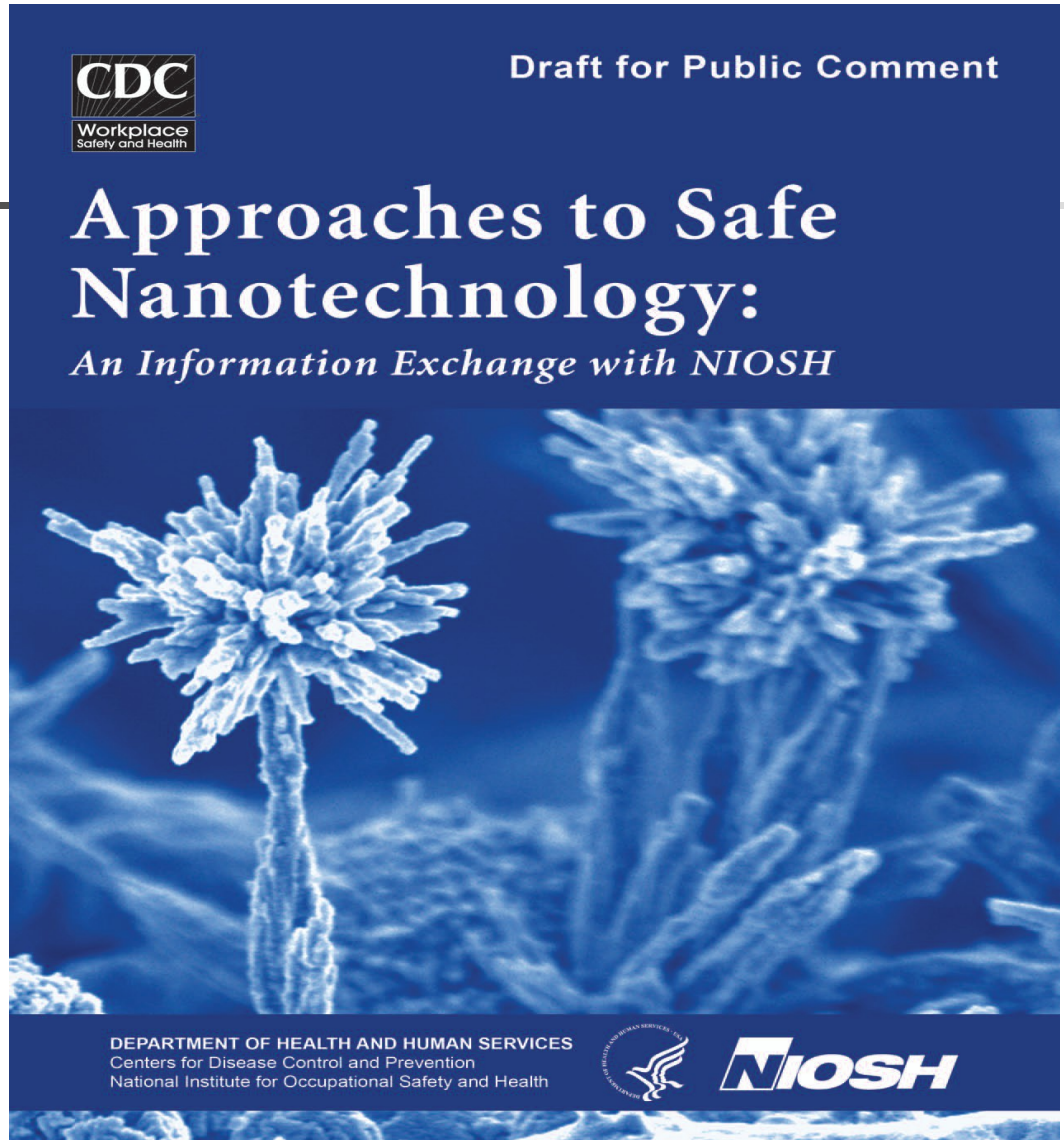
Cancer Detection

- By injecting quantum dots into tumors, investigators have been able to image sentinel lymph nodes. These results could lead to a simple, non-invasive method for detecting metastasis.
- The investigators found that they readily observed the quantum dots moving out of tumors and into the lymph system.



Environmental and Occupational Health Concerns

- Every new technology has had unforeseen impacts on Environmental and Occupational health
- The last 5 years has seen heightened OHS concerns, yet little is still known about potential risks


CDC
Workplace
Safety and Health
Draft for Public Comment
Approaches to Safe Nanotechnology:
An Information Exchange with NIOSH
DEPARTMENT OF HEALTH AND HUMAN SERVICES
Centers for Disease Control and Prevention
National Institute for Occupational Safety and Health
NIOSH

Occupational Health Concerns

- Effects of exposure are not known
- Nanomaterials are so small they interact with other substances at the quantum (atomic of subatomic) level
- They don’t behave simply like solids, liquids, or gases
- Can be inhaled or absorbed by skin through protective gloves
- Exposure control: materials must be treated as gases

What We Do Know

- Ultrafine particle research (smaller than 100 nanometers)
- Surface area and chemical chemistry versus just mass determines toxic response
- Can penetrate through skin and transfer to other organ systems than lung
- Caution in the absence of research findings

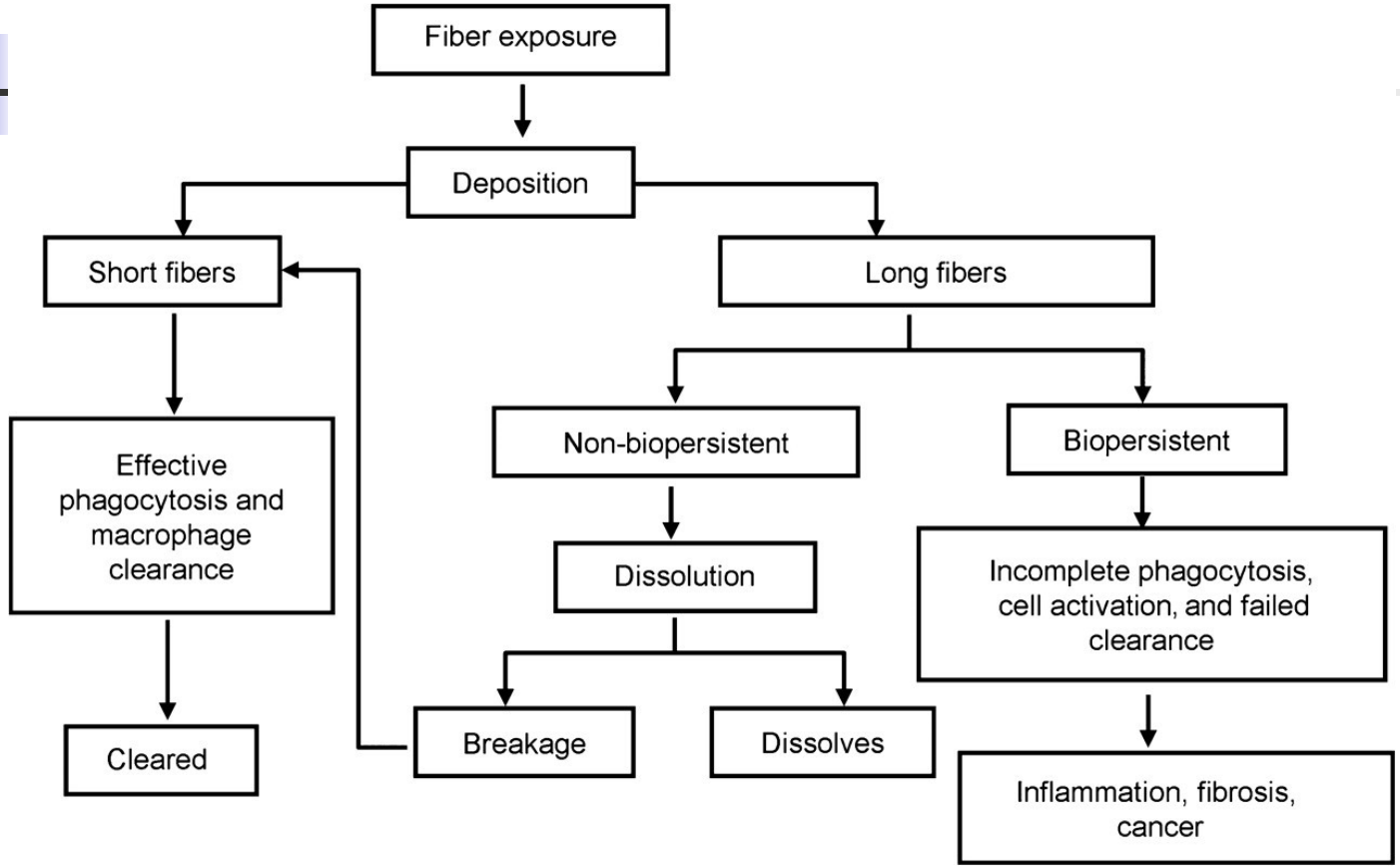
Effects on Human Health?

- How are humans exposed?
- How do they enter the body?
- Once in the body, where do they travel, and how do they interact with the body's systems?
- Will those interactions be harmless, or could they cause acute or chronic adverse effects?
- What are appropriate methods for measurement and control?

Toxicology Research Needs

- Investigating and determining the physical and chemical properties
- Evaluating short and long-term effects that nanomaterials may have in organ systems and tissues (ex: lungs)
- Determining biological mechanisms for potential toxic effects
- Determining if a measure other than mass is more appropriate for determining toxicity

Paradigm for the role of long fibers and biopersistence in the pathogenic effects of fibers

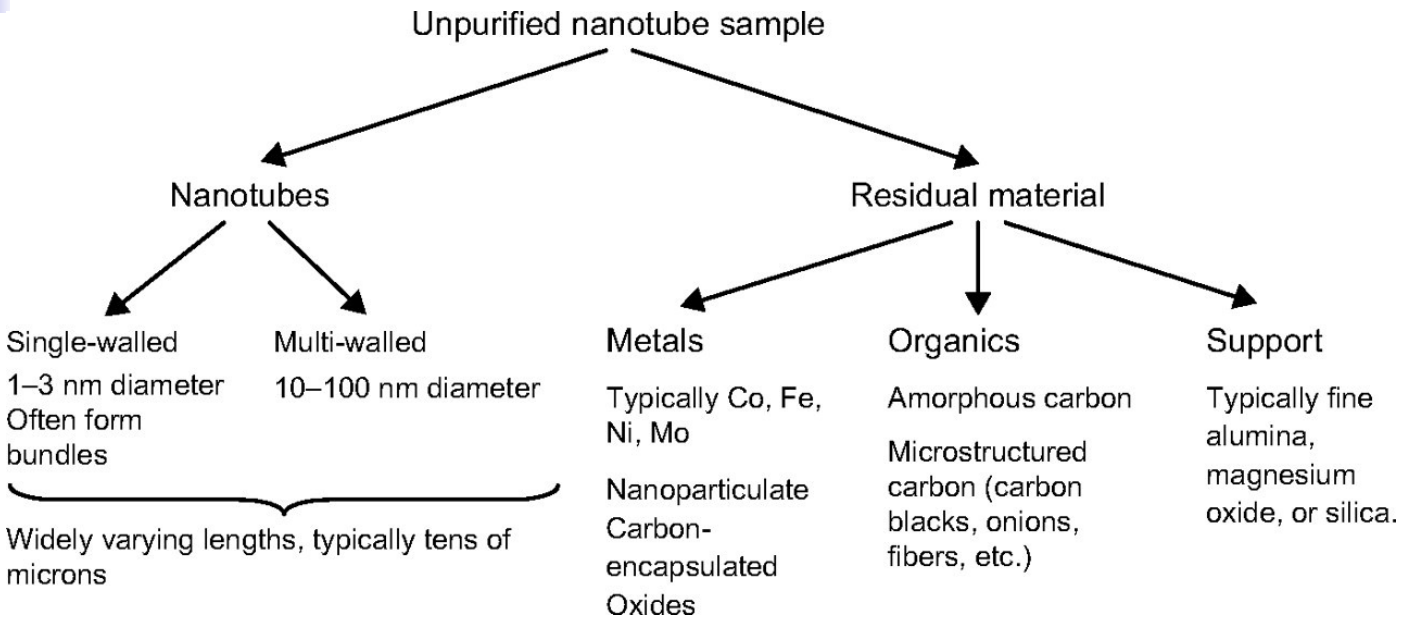


Donaldson, K. et al. Toxicol. Sci. 2006 92:5-22; doi:10.1093/toxsci/kfj130

Copyright restrictions may apply.

TOXICOLOGICAL SCIENCES

Possible components in a sample of unpurified CNT



Donaldson, K. et al. Toxicol. Sci. 2006 92:5-22; doi:10.1093/toxsci/kfj130

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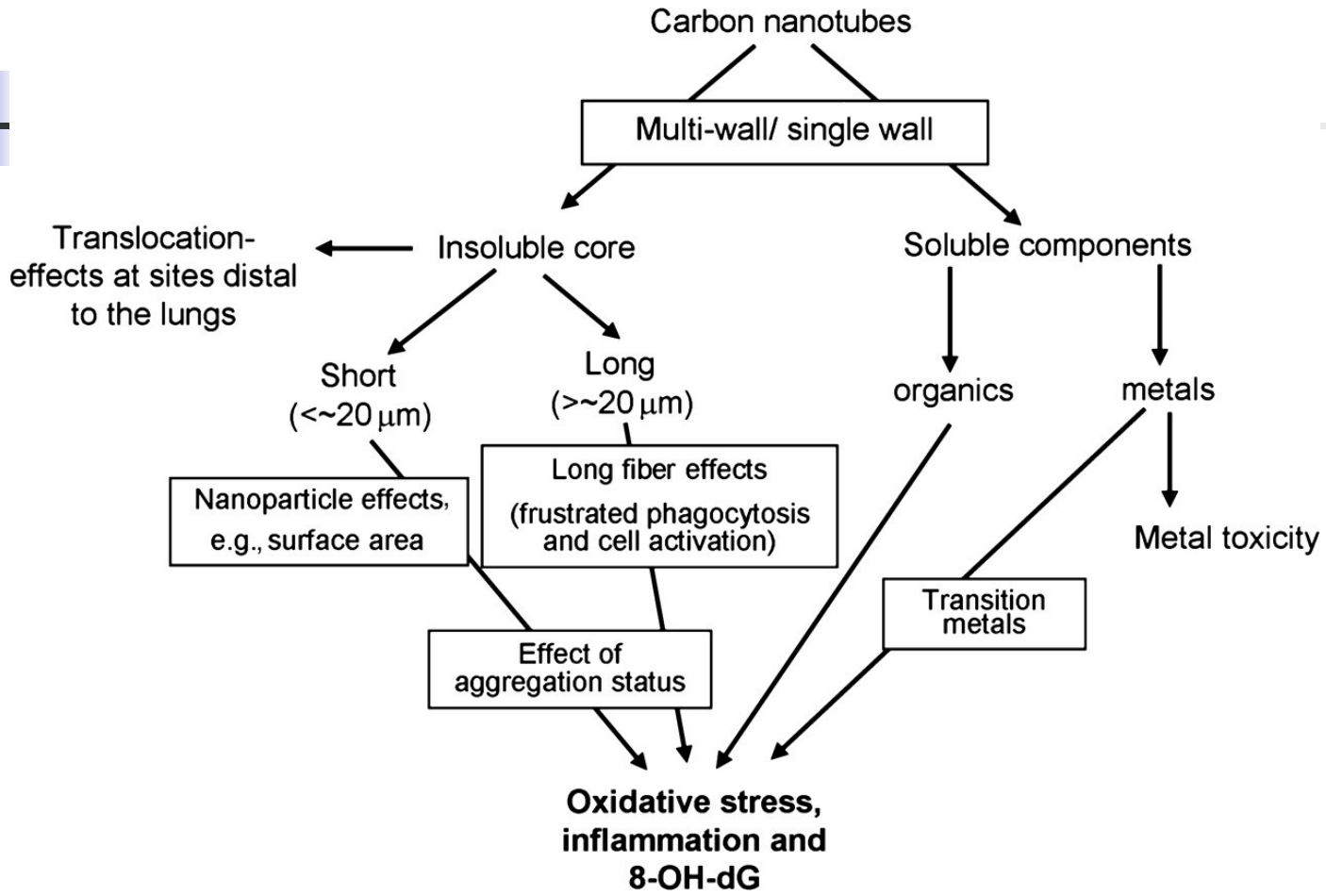
TOXICOLOGICAL SCIENCES

Important characteristics of nanotubes and their potential effects on processes that could impact on adverse effects



Donaldson, K. et al. Toxicol. Sci. 2006 92:5-22; doi:10.1093/toxsci/kfj130

TOXICOLOGICAL SCIENCES

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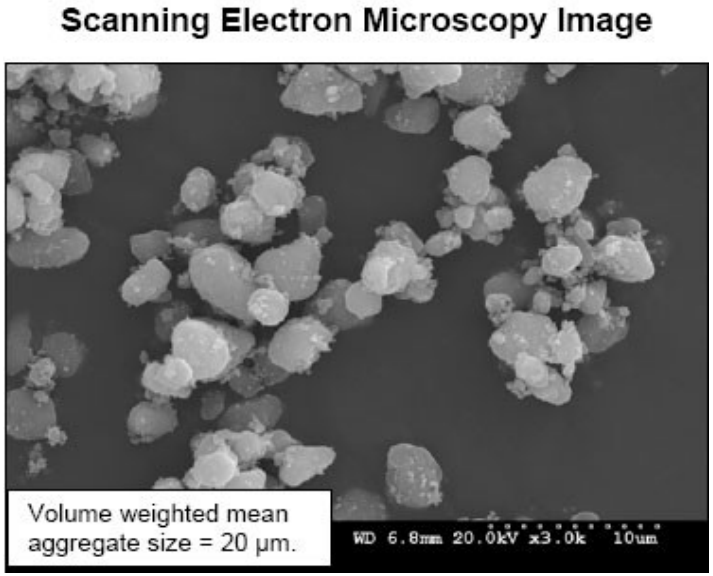
Absorption of Nanoparticles

- When inhaled, nanoparticles are deposited in all regions of the respiratory tract.
- The small size facilitates uptake into cells and into blood and lymph circulation
- Potential target sites: bone marrow, lymph nodes, spleen, and heart.
- Access to the central nervous system and ganglia via translocation along axons and dendrites
- Penetration through the skin and distribution via lymphatic channels

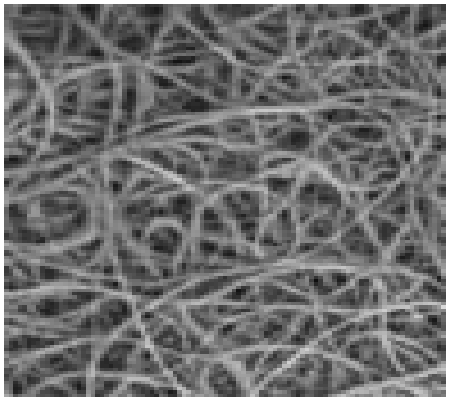
Crystaline Titanium

Anatase-sized (10 and 20 nm) TiO_2 particles in the absence of photoactivation induced oxidative DNA damage, lipid peroxidation, and micronuclei formation, and increased hydrogen peroxide and nitric oxide production in BEAS-2B cells, a human bronchial epithelial cell line.

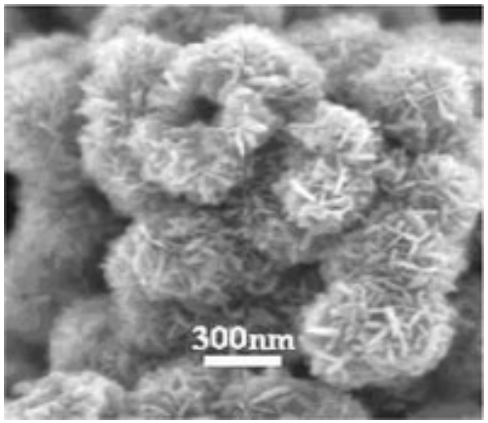


Carbon Nanotubes

Capable of producing inflammation, microscopic nodules, fibrosis, and biochemical/toxicological changes in the lungs.

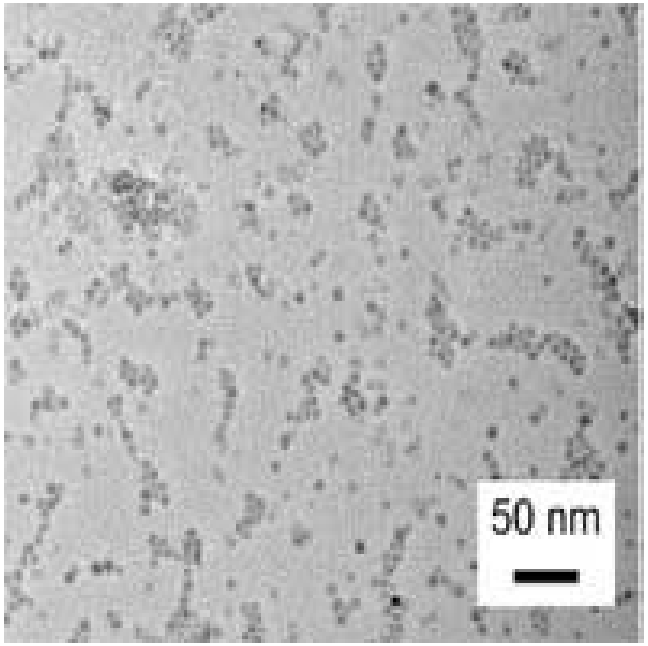


Inhalation of carbon Ultra Fine Particles alters peripheral blood leukocyte distribution with increased retention of leukocytes in the pulmonary vascular bed. Exposure also reduced the percentage of CD4(+) T cells, basophils, and eosinophils.



Cadmium Quantum Dots

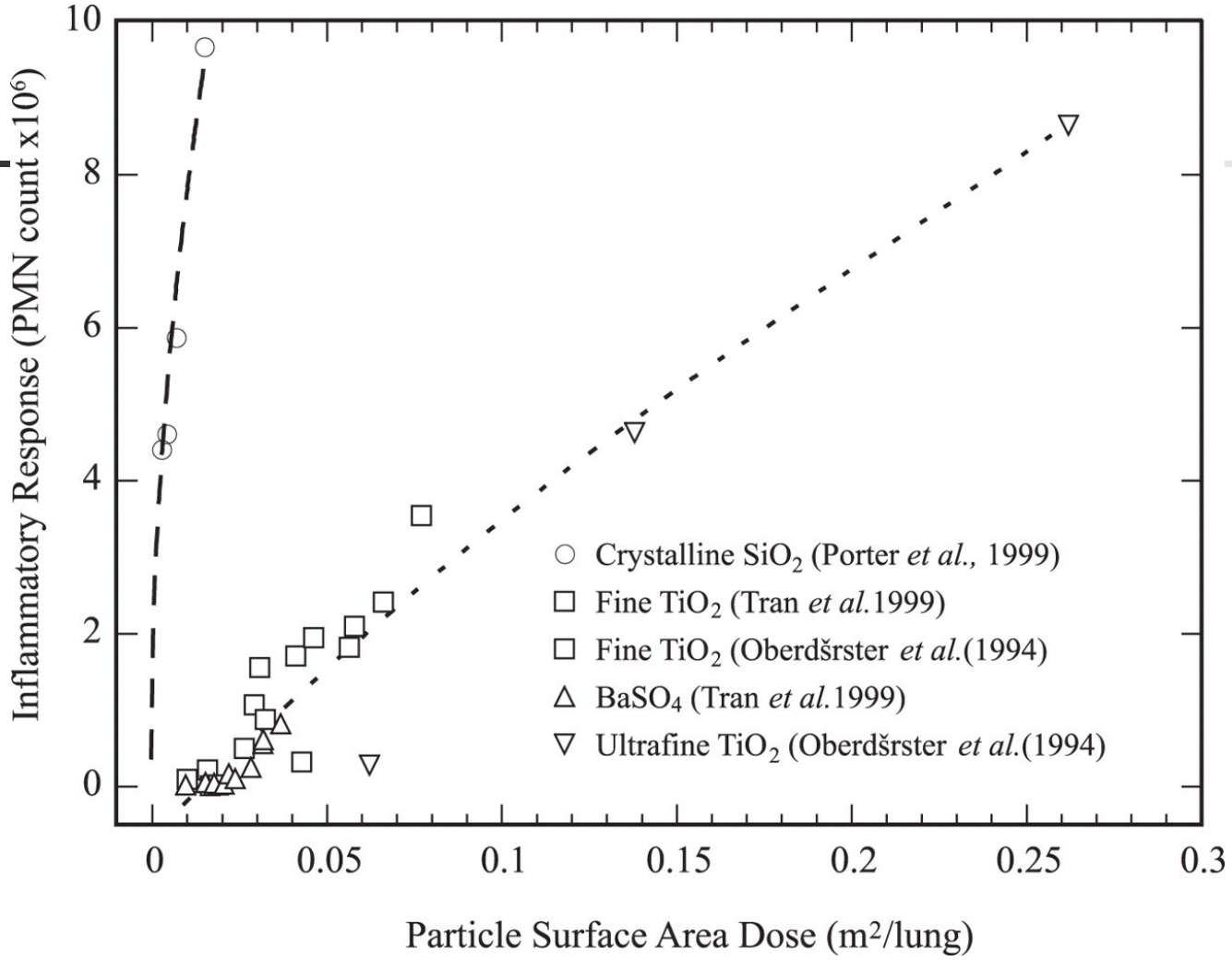
- Quantum dots of different sizes, shapes, and surface coatings can penetrate intact skin at an occupationally relevant dose within the span of an average-length work day.
- Skin is surprisingly permeable to nanomaterials and may serve as a portal of entry for localized, and possibly systemic, exposure of humans



Reactivity of Nanoparticles

- High surface area relative to volume makes them highly reactive
- Potential negatives include toxicity, induction of oxidative stress and/or cellular dysfunction
- Interaction with cells and biokinetics are different from any other man-made materials relative to larger particles

4 Pulmonary inflammatory response to crystalline silica (Porter et al., 1999), compared with TiO2 (Oberdorster et al., 1994) and BaSO4



MAYNARD, A. D. Ann Occup Hyg 2007 51:1-12; doi:10.1093/annhyg/mel071

The Annals of Occupational Hygiene

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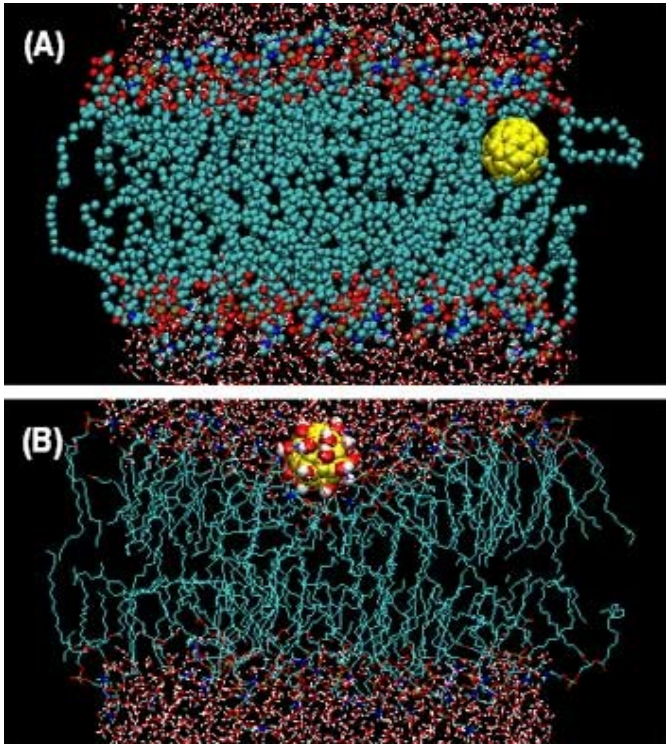
Developing Less Toxic Particles

- **Translocation of C60 and Its Derivatives Across a Lipid Bilayer (© 2007 American Chemical Society)**
- **A pristine C60 molecule can readily "*jump*" into the bilayer and translocate the membrane within a few milliseconds, the C60(OH)20 molecule can barely penetrate the bilayer**



Risk Assessment

- Determining the likelihood that current exposure-response data (human or animal) could be used in identifying and assessing potential occupational hazards
- Developing a framework for evaluating potential hazards and predicting potential occupational risk of exposure to nanomaterials

Epidemiology and Surveillance

- Evaluating existing epidemiological workplace studies where nanomaterials are used
- Identifying knowledge gaps where studies could advance understanding of nanomaterials
- Integrating nanotechnology health and safety issues into existing hazard surveillance methods and determining whether additional screening methods are needed
- Using existing systems to share data and information about nanotechnology

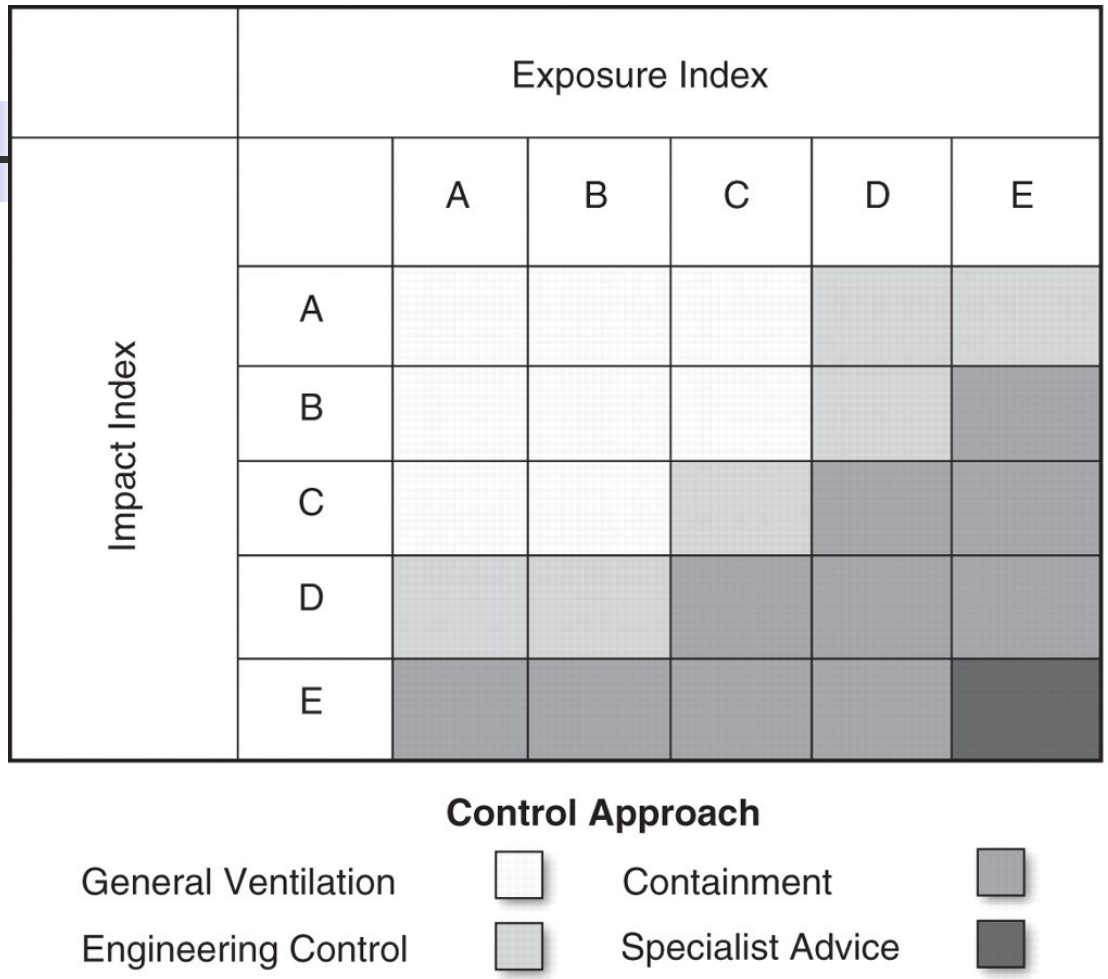
How Many Workers Are Exposed?

- No comprehensive statistics on the number of people in the U.S. who might be exposed nanomaterials
- No current, comprehensive data from official survey sources, such as the U.S. Bureau of Labor Statistics (BLS).
- The magazine SMALL TIMES has reported a partial figure. In a 2004 survey, it estimated that 24,388 people are employed in companies engaged only in nanotechnology.

Engineering Controls and PPE

- Evaluating the effectiveness of **engineering controls** in reducing occupational exposures and developing new controls where needed
- Evaluating and improving current **personal protective equipment**
- Evaluating suitability of control banding techniques where additional information is needed; and evaluating the effectiveness of **alternative materials**

7 Conceptual interpretation of how a control-banding type of approach might be applied to airborne engineered nanomaterials



MAYNARD, A. D. Ann Occup Hyg 2007 51:1-12; doi:10.1093/annhyg/mel071

The Annals of Occupational Hygiene

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Measuring Workplace Exposures

- Available devices and methods are not designed to take and analyze samples at the nano-scale.
- Uncertainties regarding the appropriate parameters for sampling and analysis. Emphasis on particle size, surface area and surface chemistry (or activity)
- Need instruments that measure particle number and surface area.

Exposure Assessment

- Determining key factors that influence the production, dispersion, accumulation, and re-entry of nanomaterials into the workplace
- Assessing possible exposure when nanomaterials are inhaled or settle on the skin
- Determining how possible exposures differ by work process
- Determining what happens to nanomaterials once they enter the body

Fire and Explosion Safety

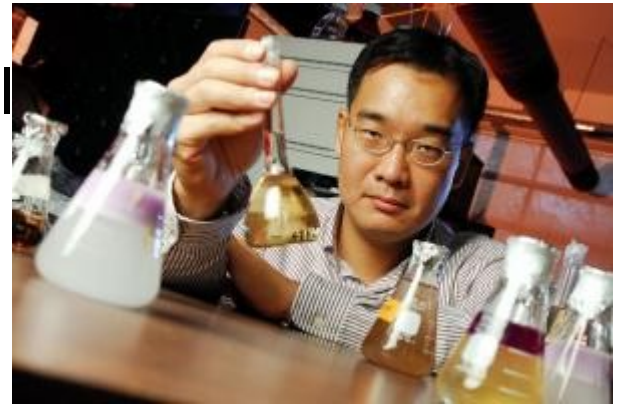
- Identifying physical and chemical properties that contribute to dustiness, combustibility, flammability, and conductivity of nanomaterials.
- Recommending alternative work practices to eliminate or reduce workplace exposures to nanoparticles.

Need to Also Consider Environmental Exposures

- Research on environmental exposures and brain penetration in large-mouth bass
- Nanoparticles used in bioremediation
- What is the environmental fate of particles?

Environmental Fate: Industrial Nanomaterials Appear Vulnerable To Dispersal In Natural Environment

- *Science Daily* — Laboratory experiments with a type of nanomaterial that has great promise for industrial use show significant potential for dispersal in aquatic environments -- especially when natural organic materials are present. Dec 23, 2006



Research Needs

- How are particles degraded in soils and water?
- What are the toxic effects of nanoparticles on aquatic bacteria?
- How do soil microbes react to and alter themselves in the presence of nanoparticles ?
- Educational outreach to promote public awareness and understanding of nanoscale science and its applications

Important Resource

- Nanoparticle Information Library (NIL)
  - Industries
  - Occupations
  - Health and Safety Issues

- http://www2a.cdc.gov/niosh-nil/index.asp

Additional Valuable Resources

- MIT Tech Review – Nanotech
  - http://www.technologyreview.com/Nanotech/
- Center for Responsible Nanotechnology
  - http://www.crnano.org/index.html
- Project on Emerging Technologies
  - http://www.nanotechproject.org/

Conclusions and Questions?

- There are no convenient methods of measuring workplace exposures
- Insufficient knowledge on the extent of exposure to nanoparticles
- Effectiveness of control measures have not been tested
- Knowledge is insufficient for risk assessment